bled by recombination between similar or identical sequences at different places in the genome? Clearly, transposons must be sequestered from the recombination machinery in some way that is at this point very poorly understood.

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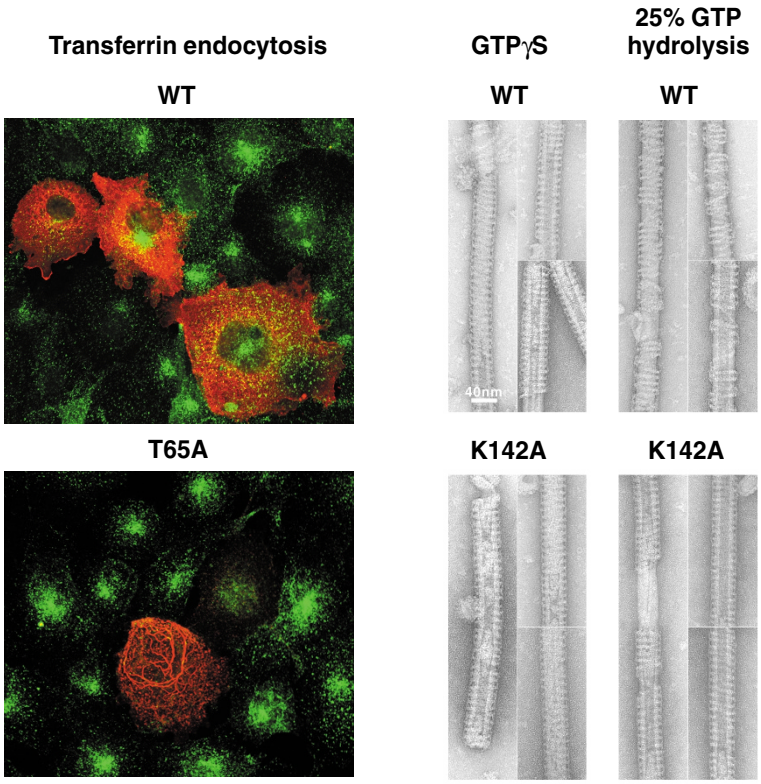
The separator

Dynamin is essential for receptor-mediated endocytosis, a mechanism by which a cell obtains nutrients (such as iron or cholesterol) from its environment. In this process, the membrane, which contains receptors and their bound ligands, folds inward to form a 'pit'; the pit then closes up to form a vesicle that breaks off from the membrane.

Dynamin oligomerizes around the neck of the pit and is involved in cutting off the vesicle from the membrane, but its exact role in the process is under considerable debate. Dynamin is a GTPase and, in principle, could provide the mechanical force — derived from GTP hydrolysis — to pinch off the vesicle from the membrane. It is also possible that dynamin functions as a classic G-protein — that is, a molecular switch that senses the state of the bound nucleotide to regulate downstream scission factor(s). In this case, GTP binding, but not GTP hydrolysis, would be sufficient for endocytosis.

To differentiate between these two hypotheses, Marks *et al.* (*Nature*, **415**, 231–235; 2001) mutated residues that may be important for the GTPase activity of dynamin. One such mutant, T65A, has an affinity for GTP similar to that of wild type but lacks the hydrolytic activity. Importantly, this mutant does not support endocytosis *in vivo* of a model substrate, transferrin (compare the cells (colored red) expressing wild type dynamin (top left) to those expressing T65A dynamin (bottom left); transferrin is highlighted green), indicating that GTP binding alone is insufficient for endocytosis.



adapted from Marks *et al.*

Another mutant, K142A, is not defective in GTP binding or hydrolysis but still does not support endocytosis. When bound to GTPγS, purified wild type dynamin assembles *in vitro* into a tight helix around lipid nanotubes (top middle). After GTP hydrolysis a concerted conformational change occurs that alters the pitch of the dynamin helix (top right). The K142A mutant can assemble into a helix similar to that of wild type in the presence of GTPγS (bottom middle); however, the conformational change after GTP hydrolysis is seriously compromised (bottom right). This observation suggests that a concerted conformational change of dynamin is also required for endocytosis. Taken together, these findings support the hypothesis that dynamin can act as a force generator to separate vesicles from the membrane. *Hwa-ping Feng*